REVIEW

Training the next generation of protein scientists

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Abstract: Carl Brändén made significant contributions in areas of protein X-ray crystallography and science education. As the 2011 recipient of the Protein Society award honoring Carl's contributions, I had the opportunity to reflect on the undergraduate educational activities that have been practiced in my own laboratory over the past 24 years at the University of Maryland Baltimore County, an institution that emphasizes both research and undergraduate education. A system has been developed that attempts to minimize the tension that can exist between conflicting graduate research and undergraduate mentoring goals. The outcomes, as measured not only by subsequent activities of the participating undergraduates, but also by the activities of the graduate students and postdocs that worked with the undergraduates, indicate a general overall benefit for all participants, particularly for women and underrepresented minorities who are traditionally poorly retained in the sciences. Greater participation of undergraduates in research activities of active scientists who often focus primarily on graduate and postdoctoral training could have a positive impact on the leaky undergraduate science pipeline.

Keywords: mentoring; undergraduates; minorities; STEM

Introduction

The ability to conduct high-quality science research is critically dependent on the quality of the future scientific talent pool. The demographics of this talent pool are changing in many nations, particularly the United States where graduate research relies increasingly on students who received their undergraduate education in other countries. According to the U.S. National Science Foundation, doctoral recipients holding temporary visas accounted for 37% of the total Science and Engineering degrees awarded in 2009, up from 27% in 1989.[1] The trends are more significant in the Physical Sciences and Engineering, where doctoral degrees to non-U.S. citizens or Permanent Residents increased from 16 to 42% and from 33 to 55%, respectively, from 1989 to

Abbreviations: PI, principal investigator; STEM, science, technology, engineering, and mathematics; URM, underrepresented racial minority (defined by the U.S. National Institutes of Health and National Science Foundation as being a U.S. citizen or permanent resident who is American Indian or Alaska Native, Black or African American, Hispanic or Latino, Native Hawaiian or Other Pacific Islander).

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2009.[1] According to a recent Survey by the Council of Graduate Schools, offers of graduate school admission to Chinese students increased by 23% from 2009 to 2010, and offers to students from India jumped by 8%.[2]

There can be no doubting the advantages associated with international graduate-level education. International applicants are typically highly competitive, and the mixing of students from different cultures provides important educational opportunities that can strengthen international understanding and collaboration. Although these activities should continue to be promoted, one cannot help but be concerned about the fact that relatively few students who receive their undergraduate education in the United States pursue advanced degrees in fields of science, technology, engineering, and mathematics (STEM). The problem is exacerbated for women and racial minorities who have been historically underrepresented in STEM fields.[1,3] Underrepresentation does not result from a lack of early student interest.[4] According to surveys of high school seniors[5] and of college freshmen,[6] similar percentages of Caucasian, Asian American and underrepresented racial minority (URM) students begin college with interests in pursuing STEM degrees, but the URM students leave STEM fields at rates that significantly exceed those of their Caucasian and Asian American peers.[6] Since Caucasians will comprise less than 50% of the U.S. population by 2050,[7] education and retention efforts need to focus more heavily on populations that are currently underrepresented in STEM fields.

Research scientists in academic laboratories could play an important role in helping to retain the brightest STEM undergraduates through normal classroom contact and by providing opportunities to participate in the scientific research enterprise. Unfortunately, contact between research active faculty and undergraduates can be limited, particularly during the early academic years when students make important decisions regarding their fields of study. Highly active research faculty often only get classroom contact with more advanced undergraduates after the freshman/sophomore "weeding" has occurred, limiting their influence on a large body of potentially impressionable students. Undergraduate mentoring can also be time consuming, not only for the Principal Investigator (PI) of the lab, but more significantly for the graduate students and postdoctoral colleagues responsible for training and working with the undergraduates. New tenure-track faculty are often advised not to work with undergraduates because doing so "can be detrimental to research productivity and progression to tenure." Summer research internships and other short-term research activities involving non-matriculated students considering careers in science can be particularly burdensome because they occur during the summer months when research activities are often at their peak. Here I describe a system that has evolved in my laboratory over the past 24 years that enables the training of relatively large numbers of matriculated and non-matriculated undergraduates, as well as high-achieving STEM-oriented high school students.

Organizational Structure

The organizational structure in my lab resembles an inverted pyramid, with the PI (me) at the bottom. My job is to ensure that the people above me have the resources they need to successfully design and conduct their experiments. I interact daily with the layer immediately above me (the graduate students and postdocs), and they interact daily with the undergraduates within their individual groups. During the summer, UMBC undergraduates interact daily with the summer-only outreach students, which include non-matriculated undergraduates from other colleges/universities and local high school students. Summer-only students also have daily meetings, as well as a variety of on- and off-campus events organized by institutional staff to promote bonding and communication and to help prepare students for college entrance exams. During the summer we have weekly lab meetings in which research presentations are given only by the undergraduates and high school students. All undergrads and high school students are required to ask questions at these meetings—the penalty for not asking a question is 20 push-ups. We also have regular informal group meetings that include seminars and discussions led by the graduate students and postdocs in the lab, and all undergraduates and high school students present research posters at the annual UMBC Summer Undergraduate Research Festival, Figure 1.

Graduate Student and Postdoc Commitments

Our system only works because the graduate students and postdocs in the lab realize significant benefits. Prospective graduate students and postdocs are informed of our undergraduate training activities before they join the lab, so to some extent I recruit senior student colleagues who have interest in working with undergraduates. A graduate student or postdoc who joins my lab typically works independently for the first several months, until promising preliminary data are obtained and a well-defined research project is established. During the first summer after joining my lab, these colleagues select two UMBC undergraduates from a pool of six to eight new students (typically rising sophomores). These undergraduates generally remain in the lab for 3 years or more and become responsible for training new UMBC undergraduates and the summer outreach students. Thus, a graduate student or

Figure 1. Group photograph taken during the summer of 2011, immediately following UMBC's Summer Undergraduate Research Festival.

postdoc is only heavily involved in basic lab training during the first summer in the lab.

Undergraduate Commitments

UMBC undergraduates who wish to work in my laboratory should have GPAs consistent with their long-term goals. Those wanting to matriculate to an MD-PhD program should have a GPA of at least 3.6, whereas students interested in medical or graduate schools should have GPAs of at least 3.4 and 3.2, respectively. Lower GPAs are acceptable, but students are first made aware that the GPA is generally the first and most influential metric used when making admission decisions. Undergraduates are generally allowed to begin conducting research in my laboratory during the summer after their freshman year. Although students often express interest in joining earlier, this general requirement allows students to focus fully on their classes during their freshman year, and since I tell students that I rarely accept students with GPAs below 3.2, it provides some level of academic motivation.

With few exceptions, all UMBC undergraduates must start their lab work in the summer—not during the academic year—and they must commit to two sequential summers of full time effort, along with 10 h per week (spread out over at least three weekdays) during the intervening academic year. Students are not permitted to take summer courses or hold hospital internships or other jobs during the summer. Under these terms, the graduate students and postdocs are much more eager to work with the undergraduates. By the end of the summer, the undergraduates are typically self-sufficient and can work effectively even while classes are in session. In contrast, the daily and weekly interruptions that occur when attempting to train undergraduates during the academic year while classes are in session typically leave both the senior colleagues and undergraduates frustrated. Historically, undergraduates who join my laboratory in the summer after their freshman year continue to work in the lab until they graduate from UMBC, and this can be a tremendous resource for the senior colleagues in the lab. The relationships that are developed typically continue well after the groups of students leave UMBC.

Undergraduates Are Trained in Pairs

Our experiences indicate that the senior colleagues spend less time retraining and reviewing concepts when students are trained in small groups. The undergraduates tend to compare their training notes, discuss questions with each other, and look up information together, which often precludes redundant explanations by the senior colleagues. Thus, training undergraduates in pairs actually reduces the teaching burden on the graduate students and postdocs, and at the same time it allows them to "grow their groups" by two individuals instead of one.

Age Does Not Matter

One home-schooled woman joined my laboratory as a 14-year old UMBC freshman. Her first co-authored paper was accepted for publication in the *Proceedings of the National Academy of Sciences* when she was 16, and her second paper (*Journal of Molecular*

Biology) was accepted when she was an 18 year-old senior leading her own group of undergraduates. She graduated from UMBC at 18 and matriculated to the MD-PhD program at Harvard, eventually with three publications from her undergraduate work at UMBC. Although most undergraduates begin working in my laboratory in the summer after their freshman year, more than a dozen initially joined my laboratory as summer high school interns aged 16 or younger.

High Expectations

Undergraduate research in my lab is a "full immersion" experience, and prospective undergraduates who interview for a position in my lab are informed upfront that recommendation letters for graduate or professional schools will be initially drafted by the graduate student or postdoc that leads their team. They thereby understand that the impression they make on the people that they work with is more important than the impression they think they are making on me, an important point since I travel frequently and am often not able to monitor laboratory participation. I also inform the prospective undergraduates that my recommendation letter for them will include comparisons with former undergraduates who graduated with very strong GPAs, co-authored multiple papers, and matriculated to top graduate and professional schools. Prospective students are made to understand that "just getting your feet wet" and hanging out in the laboratory will not be sufficient to receive even a modest recommendation letter. Students who just want to "get a feel" for research or are primarily looking for a medical school recommendation are strongly encouraged to obtain research experience elsewhere.

Making it Fun

For undergraduates who are able to make the necessary commitments, the years spent in the laboratory can be both rewarding and fun. Most undergraduates participate in at least one national or international scientific conference, and I've attended several Protein Society meetings in San Diego with groups of 6–10 students. Students not only have the opportunity to present their work at poster sessions and interact with top scientists (a first for most students), they also get to experience life in different parts of the country—including ocean kayaking with sharks and seals off the coast of La Jolla and skiing in the Rockies. In addition, we have several off-campus activities designed to promote communication and collegiality, including barbecues at my home and summer crab picnics at a local park. Many undergraduates participate in our weekly mountain bike rides, and the students themselves often participate as groups in organized intramural athletic activities. In addition, I organize a winter group retreat that is held annually near a ski resort in Maine. This event, which is generally attended by 30–40 current and former students, includes 2 days of travel (10 h each way by car or coach) and 3 days of skiing. I cover the cost of the rental house (a large old home that can accommodate the large group), and everyone chips in for food. Meals are prepared by different groups of students, at a total cost of about $40 each for the entire trip. I have found this to be a terrific venue for catalyzing discussions not only about ongoing science activities, but also about general issues and challenges that are differentially faced by the heterogeneous population of U.S. and international students in the lab.

Race and Gender

Research in my laboratory has benefited tremendously by undergraduate URM talent that has been drawn to UMBC and supported by programs established by UMBC's African American president, Dr. Freeman Hrabowski, III. Under Dr. Hrabowski's leadership, UMBC has transformed over the past 24 years from an institution in which many URM students felt under-supported (in 1987, when I arrived on campus, African American students held a sit-in protesting their view that the STEM faculty was racially biased) to one that now receives national recognition for it's STEM diversity efforts and accomplishments (for examples, see Refs. 8–10). Noteably, URM students who have participated in UMBC's Meyerhoff Scholars Program are twice as likely to graduate with a STEM degree, and six times more likely to pursue a graduate STEM degree, than URM students with similar interests, preparation, and high school academic performance who turned down Meyerhoff offers to attend other universities.[3,11–13] My laboratory has benefited significantly from this pipeline: More than 40% of the 200+ undergraduates that have worked in my laboratory are from racial groups that are underrepresented in the sciences (mainly African American), and more than 60% of the students were female. These students were not selected to join my laboratory for charitable considerations – they were selected because of their talent. For example, African American twins who worked in the lab during all 4 years of college graduated with near-perfect GPAs (one was a UMBC Valedictorian), published five papers, and matriculated to Harvard medical school. Another African American UMBC Valedictorian with undergraduate publications matriculated to the MD-PhD program at Harvard/MIT. In fact, a large fraction of the URM students and women who have worked in my lab matriculated to PhD, MD-PhD and professional schools at top U.S. institutions including Harvard, Yale, U.C. Berkeley, Washington University, the University of Pennsylvania, and other top-ranked U.S. institutions (see below).

What is the difference between my lab and many other laboratories that involve undergraduate researchers? Perhaps the biggest difference is the number of URM and female undergraduates, which is large enough to generate a sense of community. The undergraduate presence actually dominates the lab, which typically includes 2–3 postdocs, 4–6 graduate students, and 12–18 undergraduates during the academic year. During the summer, because of our outreach efforts, the number of undergraduates and high school students in the lab often swells to 25–30 students.

A second major factor is that we have regular (almost daily) discourse on subjects that are sometimes considered taboo or that at least can raise levels of discomfort. Students are routinely prodded about their views on race, religion, and politics during our lunchtime gatherings (undergraduates are encouraged to come back to the lab for their lunch, even if they are not working in the lab that day, so that they can keep up with the day-to-day progress within their groups). Although these conversations can sometimes lead to indigestion, they almost always open doors for better communication and understanding. Within the past 5 years, my lab has included Jewish undergraduates working with a Palestinian postdoc, undergraduates from Bosnia and Serbia working together on a team, and of course, mixtures of African Americans, Caucasians and Asians on nearly all teams of students. We talk openly about the political, racial, and socioeconomic issues of the times—a practice that I believe has led to strong working relationships, better communication, and an overall atmosphere of inclusiveness rather than simply tolerance.

Sources of Funding

Although a few undergraduates have worked for academic credit only, most begin working at the minimum wage level of support. Many students who have worked in my lab are first-generation college students who would otherwise have to seek other employment. In addition, salary can be a good motivator when experiments are not working as expected.

The majority of students who have worked in my lab were supported by my R01 NIH grants. I include undergraduate support as line items on both of my currently active R01 NIH grants (each of which supports seven undergraduates), and the undergraduate support and participation has been uniformly praised by the NIH Study Sections that have reviewed the grants. Some undergraduates have been supported by training grants to UMBC to promote undergraduate STEM education and diversity. UMBC currently receives funding from the MORE Division of the National Institute of General Medical Sciences and the Howard Hughes Medical Institute, both for campus diversification efforts—most of which is used for student salaries.

Outcomes

Over the past 20 years, our lab has introduced more than 250 undergraduate and high school students (186 UMBC undergraduates in long-term research projects, 20 non-UMBC summer undergraduates, and 45 high school students) to biomedical research. Of the 206 undergraduates, 90 (44%) are from URM groups (nearly all African Americans) and 120 (58%) are female. A total of 39 undergraduates are currently pursuing their undergraduate degrees, and of the 167 students who have already received undergraduate degrees, 46 are in or have graduated from PhD programs (27 URM), 11 are in or have graduated from MD-PhD programs (8 URM), and 44 are currently in or have graduated from MD programs (16 URM). Thus, about 40% of the undergraduates who worked in my laboratory have or are working toward postgraduate degrees. Of the 90 URM undergraduates who have worked in my lab and have graduated, 35 (40%) are pursing PhD or MD-PhD degrees and 16 (18%) are pursuing medical degrees. The undergraduates have contributed significantly to the research productivity of the lab: a total of 61 undergraduates (28 URM and 37 women) have co-authored 38 peer reviewed research articles.

A total of 27 graduate students (9 URM; 16 women) have earned PhD degrees, and 5 additional students (4 URM, 4 women) have earned Masters Degrees. Of the 27 PhD graduates, 7 currently hold postdoctoral positions (4 URM, 7 women), and 9 hold tenured or tenure-track faculty positions (3 URM, 2 female). Of the 19 postdoctoral associates (3 URM, 12 women) who have left my laboratory, 8 hold tenured or tenure-track faculty positions (1 URM, 4 female). Thus, of the 15 former graduate students who have completed their postdoctoral training and 19 former postdoctoral associates, 17 now hold tenured (11) or tenure-track (6) faculty positions at PhD-granting institutions including Harvard, University of Virginia, Ohio State, Kansas University, Iowa State, and Miami of Ohio, among others. Three additional former colleagues hold non-tenured college teaching positions and two former MD-PhD students hold medical residency positions.

Summary

The involvement of large numbers of undergraduates has been a win-win for the lab. The undergraduates benefit from the experience, income, and academic and professional support network, and the graduate students and postdoctoral fellows benefit by the long-term commitment of "extra hands" and the mentoring experiences. The undergraduates add a dimension of energy and creativity that might not exist in a smaller research setting comprising only graduate students and postdocs. Undergraduate participation has certainly not been "detrimental" to our research activities, as R01 NIH funding on two projects has been maintained for more than 20 years, and the lab has been supported by HHMI through four cycles of competitive review. In fact, the undergraduates have contributed significantly to our productivity, having co-authored ~65% of the research articles that have been published from my laboratory over the past 10 years.

In the long term, the field of Protein Science, and STEM in general, will only be as good as the talent pool that we are able to attract and retain. Greater participation of undergraduates in high-level federally funded research activities is one approach that could help stabilize and enhance the STEM pipeline.

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